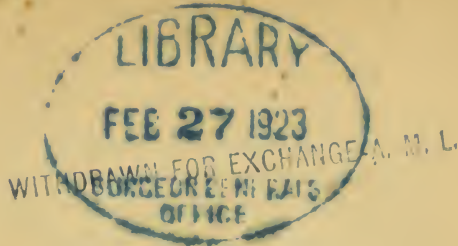


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# United States Department of Agriculture,

BUREAU OF CHEMISTRY—Circular No. 39.

H. W. WILEY, Chief of Bureau.

## GENERAL RESULTS OF THE INVESTIGATION SHOWING THE EFFECT OF BENZOIC ACID AND BENZOATES UPON DIGESTION AND HEALTH.<sup>a</sup>

### INTRODUCTION.

In the continuation of the work described in Parts I to III of this bulletin, experiments were conducted, according to the general plan already described, to determine the effects of benzoic acid and benzoates upon health and digestion. This investigation is of special importance because of the opinion held by many manufacturers, food officials, and consumers that benzoic acid and benzoates are probably the least harmful of the preservative substances employed. It is believed that for this reason there has been a very large increase in the use of these preservatives in the last few years, with a corresponding decrease in the amount of other preservative substances employed. It has also been claimed that there can be no reasonable objection to the use of benzoic acid by reason of its natural occurrence in many food products, either in traces or in considerable quantities. Among the products cited the cranberry occupies the most prominent position because of the notable amount of benzoic acid it contains. These considerations, however, had no determining influence on the choice of this substance for the experimental work, inasmuch as it was in-

<sup>a</sup> By reason of the restrictions placed by law upon the printing and distribution of bulletins exceeding 100 pages, it is not possible to supply the demand for Bulletin 84, Influence of Food Preservatives and Artificial Colors on Digestion and Health, from the regular edition. In order to give as wide a circulation as possible to the results of the experimental work, it has been deemed advisable, in the case of Part IV, on Benzoic Acid and Benzoates, as in preceding studies on boric acid and borates, salicylic acid and salicylates, sulphurous acid and sulphites (Circulars 15, 31, and 37, respectively), to publish the results in the form of a circular for general distribution.

cluded in the original scheme which was prepared before the work reported in Part I was begun.

The same principles which guided the organization of the work as described in Part I were followed in the present instance. Upon the selection of the members of the hygienic table each man was subjected to a thorough medical examination of the character already described. No one was admitted to the table who was suffering from any organic disease, who manifested any tendency to hereditary disease, or who had been seriously ill within the year previous to the beginning of the experimental work.

The delay which has attended the presentation of this report for publication has been due to several causes. First, the great burden of collating the data, condensing the analytical tables, and checking the data for accuracy, required, as is usual in such cases, a large amount of time and expert labor. There were also a number of points brought out in the investigations which required further study of the question, both experimentally and in consulting authorities thereon.

Another reason for the delay consisted in the fact that various representations were making on the part of manufacturers and others respecting the effect upon the industries using benzoic acid should the conclusions reached in this report receive executive and judicial confirmation. It was thought advisable, therefore, to give ample time to the industries involved to experiment with methods of manufacture looking to the elimination of objectionable preservatives. Investigations were also undertaken by this Bureau in collaboration with the manufacturing interests along the same line. Results of these investigations have shown that there is not a single article of food which has been commonly preserved by means of benzoic acid or benzoate of soda which can not be preserved and offered to the consumer in perfect condition without the aid of any chemical preservative. This fact has been completely demonstrated in the case of cider and grape juice, mince-meat, jelly, jams, catsups, preserves, and other articles of the same character, and there seems, therefore, to be no longer any industrial reason for delaying publication even if the former necessity for such delay be admitted.

It is believed that the distribution of the results of this investigation at the present time will neither work hardship to any manufacturing interest nor interfere in any way with any legitimate business. At the same time it will indicate to the manufacturer, as well as to the consumer, the important truth that the use of benzoic acid or benzoate of soda as a preserving medium is not without danger, that its effects are always injurious or tend to injury, and that its exclusion from food products is desirable not only in order to conform to the food and drugs act but also for hygienic reasons.

The greater care which is required in the manufacture of food products without the use of benzoic acid or benzoate of soda, necessitating the use of a higher quality of raw material, will place the industries which would otherwise use these preservatives in foods on a better plane, and secure for their products a greater consumption.

#### ADMINISTRATION OF THE PRESERVATIVE.

In Table I are recorded the dates of the periods and subperiods during which this experiment was conducted. A preliminary or relaxation period of one month elapsed between the close of Series VII and the beginning of Series VIII, the subjects being the same in both series, with the exception of No. 4.

TABLE I.—*Dates of periods and subperiods in Series VIII.*

Period and subperiod.	Date of beginning.	Date of ending.
	1904.	1904.
Fore period.....	Apr. 11	Apr. 20
First subperiod.....	do	Apr. 15
Second subperiod.....	Apr. 16	Apr. 20
Preservative period.....	Apr. 21	May 10
First subperiod.....	do	Apr. 25
Second subperiod.....	Apr. 26	Apr. 30
Third subperiod.....	May 1	May 5
Fourth subperiod.....	May 6	May 10
After period.....	May 11	May 20
First subperiod.....	do	May 15
Second subperiod.....	May 16	May 20

In Table II is given a schedule of the administration of the preservative. The sodium benzoate used is calculated in the table as benzoic acid. The preservative was given in all cases in capsules, as experience had shown this to be the best method from every point of view of administering a substance of this nature.

In the first preservative subperiod there was given to Nos. 1 to 6, inclusive, 1 gram of benzoic acid per day; to Nos. 7 to 12, inclusive, 1 gram per day, with the exception of the first day, when only 0.9 gram was given. During the second preservative subperiod 1.5 grams of benzoic acid were given each day to each member. In the third preservative subperiod 2 grams and in the fourth 2.5 grams were given each day, with the exceptions noted in the table. There were several cases during the fourth subperiod when the preservative, by reason of its ill effects and for other causes, had to be withdrawn. The maximum quantities of benzoic acid, therefore, given during the entire preservative period are 35 and 34.9 grams, and only three men were able to take these amounts. In all of the other cases it was necessary to withdraw a portion or all of the preservative, for the reasons already stated.



TABLE II.—*Schedule of administration of preservative, Series VIII.*  
[In capsules.]

Period and date.	Benzoic acid.						Sodium benzoate (expressed as benzoic acid).					
	No.1.	No.2.	No.3.	No.4.	No.5.	No.6.	No.7.	No.8.	No.9.	No.10.	No.11.	No.12.
First subperiod:	<i>Gms.</i>	<i>Gms.</i>	<i>Gms.</i>	<i>Gms.</i>	<i>Gms.</i>	<i>Gms.</i>	<i>Gms.</i>	<i>Gms.</i>	<i>Gms.</i>	<i>Gms.</i>	<i>Gms.</i>	<i>Gms.</i>
April 21, 1904.....	1	1	1	1	1	1	0.9	0.9	0.9	0.9	0.9	0.9
22, 1904.....	1	1	1	1	1	1	1	1	1	1	1	1
23, 1904.....	1	1	1	1	1	1	1	1	1	1	1	1
24, 1904.....	1	1	1	1	1	1	1	1	1	1	1	1
25, 1904.....	1	1	1	1	1	1	1	1	1	1	1	1
Total per individual.....	5	5	5	5	5	5	4.9	4.9	4.9	4.9	4.9	4.9
Second subperiod:												
April 26, 1904.....	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
27, 1904.....	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
28, 1904.....	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
29, 1904.....	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
30, 1904.....	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total per individual.....	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Third subperiod:												
May 1, 1904.....	2	2	1	2	2	2	2	2	2	2	2	2
2, 1904.....	2	2	0	2	2	2	2	2	2	2	2	2
3, 1904.....	2	2	0	1.5	<sup>a</sup> 1	2	2	2	2	2	2	2
4, 1904.....	2	2	0	2.5	1	2	2	2	<sup>a</sup> 2	2	2	2
5, 1904.....	2	2	0	2	2	2	2	2	2	0	2	2
Total per individual.....	10	10	1	10.0	8	10	10	10	10	8	10	10
Fourth subperiod:												
May 6, 1904.....	2.5	2.5	0	2.5	2	0	1.5	2.5	0	0	2.5	0
7, 1904.....	2.5	0	0	2.5	1	0	2.5	2.5	0	0	0	0
8, 1904.....	2.5	0	0	2.5	0	0	2.5	2.5	0	0	0	0
9, 1904.....	2.5	0	0	2.5	0	0	0	2.5	0	0	0	0
10, 1904.....	2.5	0	0	2.5	0	0	0	2.5	0	0	0	0
Total per individual.....	12.5	2.5	0	12.5	3	0	6.5	12.5	0	0	2.5	0
Total per individual for entire preservative period.....	35.0	25.0	13.5	35.0	23.5	22.5	28.9	34.9	22.4	20.4	24.9	22.4

<sup>a</sup> Took preservative, but became sick immediately afterwards.

### SUMMARY OF RESULTS.

#### MEDICAL AND CLINICAL DATA.

The observations made show that both benzoic acid and benzoate of soda, when administered to healthy young men in the quantities described, produce marked symptoms of discomfort and malaise in the majority of cases. There was little difference noted in the effect of the two forms of the preservative in the production of these symptoms. The most common symptoms are nausea and headache, which occurred in nine and eight cases, respectively. The nausea resulted in vomiting in only three cases. Seven of the subjects complained of weakness and also of burning and irritating sensations in the esophagus. Hunger was increased in three cases, and indigestion was especially noted five times.

The fact that these symptoms were not produced in all cases illustrated a point prominently brought out in the previous investiga-

tions, namely, the different degrees of toleration of the substance administered in different individuals. It should not be forgotten that the subjects upon whom the experiments were made represent the highest type of health and resistance. Hence, it is fair to infer that with less resistant types, such as children and persons with weak stomachs or other disorders of the digestive functions, or those suffering from impaired vitality in any form, the effects of the administration of the drug would have been more pronounced. It is evident, therefore, that the administration of both benzoic acid and benzoate of soda results in serious disturbances of the digestive functions, with positive indications of illness, which may easily be increased to nausea and vomiting, while headache is a very common symptom, developed together with a feeling of physical weakness and an unfitness to perform ordinary work.

#### BODY WEIGHT.

A study of the figures shows that in the case of the subjects who received benzoic acid there was an average loss of weight during the preservative period of about half a kilogram, or slightly more than 1 pound, and an additional loss during the after period of 0.46 kilogram, again a loss of about a pound. The loss in weight of those who received benzoate of soda was very much less, amounting to 0.22 kilogram, or about 0.5 pound, during the preservative period, and an additional loss of about 0.36 kilogram during the after period, making altogether a total average loss of 1.3 pounds for the entire observation. This illustrates a fact which is brought out in nearly all of the other studies, namely, that while the immediate effect of benzoate of soda on the metabolic activities was less marked than that of benzoic acid, the effect after the withdrawal of the preservative was more pronounced, so that the final result was almost as injurious as that produced by the benzoic acid alone. These facts are graphically set forth in the accompanying charts.

The final conclusion which is drawn from a study of these data is that the administration of benzoic acid as such, or sodium benzoate, in the quantities mentioned, produces a condition of the digestive activities which causes a loss in the weight of the body. In other words, the activities of a katabolic nature, which result in the destruction and excretion of tissue, are greater than those of an anabolic nature, which build up the tissues. This effect does not cease immediately upon the withdrawal of the preservative, but is continued in the majority of the cases throughout the entire after period. Hence, it is evident that the administration of these drugs in foods tends to derange the normal activities of the body and to cause a loss of tissue, resulting not only in disturbances of health but also in actual decrease in the weight of the body.

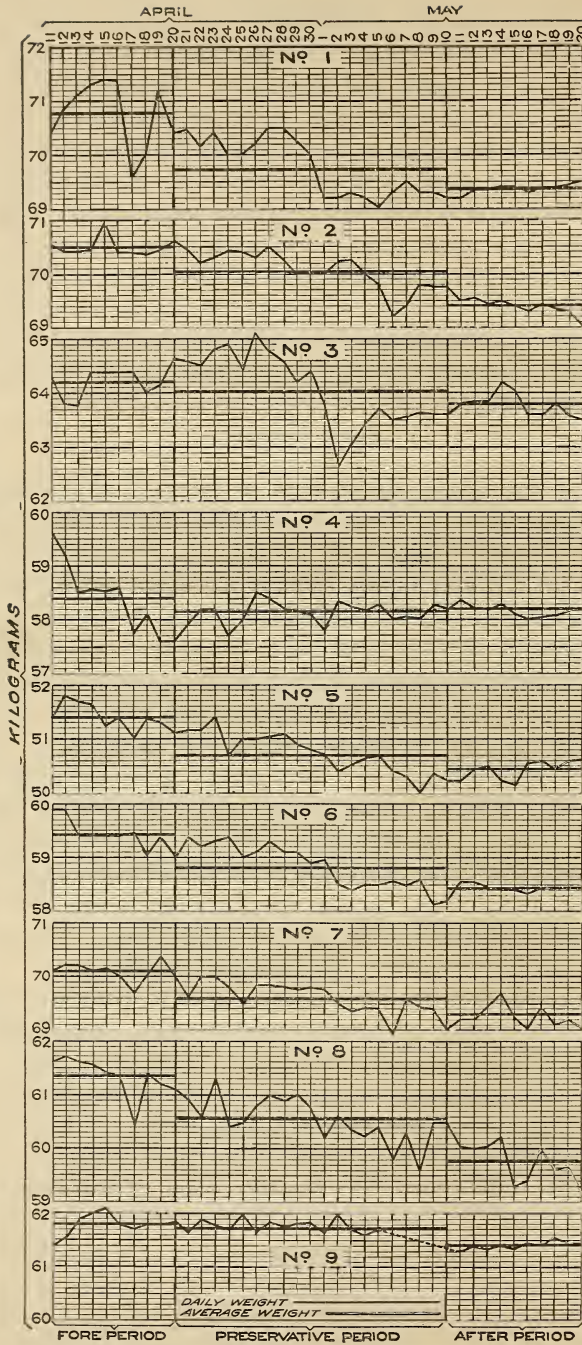


FIG. 1.—Average body weights for Series VIII, Nos. 1-9.



## EXCRETION OF BENZOIC AND HIPPURIC ACIDS.

Hippuric acid is the most important natural constituent of the urine of herbivorous animals whose food contains large quantities of aromatic substances which, either by oxidation or reduction, are converted into bodies containing the benzene nucleus. The benzene nucleus by combination with glycooll is converted into hippuric acid, in which form it is excreted. Hippuric acid is a normal con-

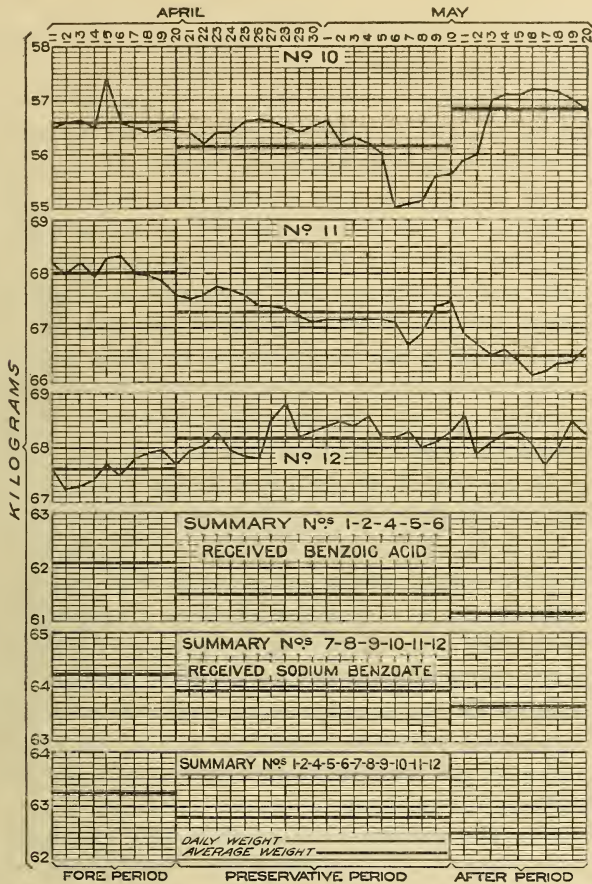


FIG. 2.—Average body weights for Series VIII, Nos. 10-12, and summaries.

stituent of the urine and the data show a fact, already well recognized by physiologists, namely, that the administration of benzoic acid or benzoate of soda to the human animal increases the quantity of hippuric acid so excreted. The limit of conversion of benzoic acid into hippuric acid is determined by the quantity of available glycooll. Any excess of benzoic acid over the quantity which can thus be converted into hippuric acid is excreted as benzoic acid.

In the original experiment the total benzoic acid recovered (both as hippuric and as benzoic acid) amounts in the case of those receiving benzoic acid to 81.32 per cent of the total quantity ingested, while for those receiving sodium benzoate the total quantity amounts to 61.41 per cent. Thus there is shown a marked tendency to restrict the excretion of benzoic acid when administered as benzoate of soda, the total decrease being almost exactly 20 per cent as compared with the excretion of benzoic acid. It is thus seen that much larger quantities of benzoic acid are retained in the system after a given time when administered as benzoate of soda than when administered as benzoic acid. This fact is another confirmation of what is shown in so many other instances in this study of the retarded effect of the preservative upon the system when administered as benzoate of soda.

The results of the supplemental study conducted with six subjects over a period of 29 days (a fore period of 5 days, a preservative period of 10 days, and an after period of 14 days) and a smaller ingestion of the preservative (a total of 12.5 grams) again showed the slower elimination of the preservative when administered as benzoate of soda. During the preservative period 93 per cent of the amount ingested as benzoic acid was recovered as hippuric acid, while for those receiving benzoate of soda only 72 per cent was recovered. The differing conditions of the experiments, especially the decreased amount of preservative and the fact that the analyses in the second case were made on the daily samples instead of the composites, account largely for the fact that all of the benzoic acid was recovered as hippuric acid in the supplemental study. At the close of the first after subperiod the entire amount of benzoic acid ingested as such had been recovered, while in the case of those receiving benzoate of soda only 76 per cent had been recovered. The increased excretion of hippuric acid as compared with the fore period continued in the case of these subjects in the second after subperiod, but only reached 77.6 per cent of the amount ingested. There is in this series, as in the preceding one, about 20 per cent less of the benzoic acid recovered when it is ingested as sodium benzoate.

The increase in the quantity of hippuric acid produced and excreted can not be neglected in studying the effects of the administration of preservatives upon health and digestion. The preservatives can only be regarded as foreign bodies of a toxic character which the system must eliminate. The normal burden imposed upon the kidneys in the excretion of the natural degradation products of metabolism is quite sufficient for the preservation of their healthy activity. The additional amount of excretory matter produced by the

administration of benzoic acid in any form can only be regarded as an unnecessary burden.

#### COMPOSITION OF THE FECES.

In the case of the young men who received benzoic acid a slight increase in the weight of the moist feces is shown in the preservative period, together with a slight decrease in the percentage of moisture therein and, of course, a corresponding increase in the weight of the dry feces. In the after period there is a marked loss in the weight of the moist feces and a continued diminution in the percentage of moisture, while the weight of the dry feces is slightly decreased, returning to the amount found in the fore period. These data show that the effect of the benzoic acid was to inhibit slightly the absorption of food material from the alimentary canal and thus to increase the quantity of feces excreted.

In the case of the young men receiving the benzoate of soda the data show a slight increase in the weight of the moist feces, and also of the percentage of moisture therein, while the amount of dry feces excreted is the same as in the fore period. In the after period there is a marked increase in the weight of the moist feces, with little change in the water content, and a correspondingly marked increase in the weight of the dry feces excreted. The benzoate of soda, therefore, appears to have had no immediate effect upon the absorption from the alimentary canal, but upon the withdrawal of the drug a diminished absorption took place. This is another indication of the retarded effect of the benzoate of soda. In almost every instance the data submitted show that the effect of the benzoate of soda upon the system is less marked and is produced more tardily than in the case of the benzoic acid. These data do not show that the preservative has produced any marked effect of a systematic character upon the weight and water content of the feces. The average weight of dry feces per man per day increased very slightly (1 gram) in the preservative period in the case of those receiving benzoic acid, and 3 grams in the after period in the case of the six men who received benzoate of soda. While these data are not sufficiently marked to demonstrate a distinct effect produced by the preservative, still the small average increase in the feces in connection with the loss of body weight would indicate a tendency on the part of the preservative to decrease assimilation.

#### THE URINE.

##### VOLUME, SPECIFIC GRAVITY, AND TOTAL SOLIDS.

The summary of the data for the men receiving benzoic acid shows a very slight decrease in the volume of the urine with a slight increase



in its specific gravity, and an increase in the total solids in the preservative period followed by a decrease in the after period.

In the case of the subjects who received benzoate of soda there is also observed a slight decrease in the volume of the urine during the preservative period, but the volume in the after period remains practically unchanged as compared with the preservative period. The specific gravity is slightly higher in the preservative period than in either the fore or after period.

The total solids in the urine of those receiving benzoate of soda are markedly increased during the preservative period, and fall again in the after period, but do not reach the figure obtained in the fore period. The data show but little influence upon the volume of the urine due to the preservative, especially as during the progress of the experiment the weather was growing warmer, and this naturally would cause a slight decrease in volume. There is, however, a marked tendency shown to increase the amount of total solids excreted under the influence of the preservative.

It is evident that neither benzoic acid nor benzoate of soda has any diuretic effect, but their influence in promoting the degradation of the tissues of the body—that is, in increasing katabolic activity—is plainly marked by the increase in the total solids excreted in the urine, although the volume of the urine is slightly diminished.

#### SULPHUR.

Under the administration of the preservative in both forms there is a slight tendency to decrease the excretion of sulphur and phosphoric acid in relation to the quantity of nitrogen excreted, while no effect is produced upon the excretion of sulphates in the urine as compared with the nitrogen excreted, due to the fact that the inorganic sulphates and the nitrogen in the urine increase in about the same ratio.

In general, there is practically no difference in the effect produced by the preservative in the two forms on the excretion of sulphur in the urine. A slight tendency is manifested in both cases to increase the katabolic activities as shown by the greater excretion of metabolized sulphur in the preservative period. This increase is the more pronounced when the diminution in the sulphur ingested is considered. The amount of neutral sulphur eliminated decreases throughout the observation, while the ethereal sulphates are remarkably constant. It is evident, therefore, that the increased excretion of total sulphur is entirely in the inorganic form, which, considered in connection with the decrease in body weight, would lead to the conclusion that the preservative tends to increase sulphur katabolism.



## MICROSCOPICAL EXAMINATION OF THE URINE.

The data relating to the microscopical examination of the urine show that the relative occurrence of microscopic bodies in the fore period, preservative period, and after period is represented by the numbers 64.44, 75.24, and 59.13, respectively. These figures indicate a tendency on the part of the benzoic acid and the benzoate of soda to increase the presence of these microscopic bodies during the preservative period. This is an indication of the effect of these bodies to increase the renal activity.

A general survey of the individual data does not show a marked effect in the case of all these bodies, but the epithelial cells, mucous strands, and mucous cylindroids are most markedly increased. The activities of the kidneys are, therefore, undoubtedly greater during the preservative period, owing to the additional amount of labor which they are called upon to perform in eliminating the products of tissue degradation. The microscopical examination of the urine, therefore, further indicates the deleterious effects of both benzoic acid and benzoate of soda on metabolism.

## MICROSCOPICAL EXAMINATION OF THE BLOOD.

In making the investigations in connection with the influence of benzoic acid and benzoates no particular significance was attached to the blood count, and for this reason the microscopical examinations were confined to one test in each of the three periods—fore, preservative, and after. The results of the examinations, however, are so significant as to render necessary another study in greater detail, which will be undertaken as soon as possible. The limited data obtained show a marked tendency on the part of the benzoic acid to diminish the number of red corpuscles in the blood (an average decrease per man of 370,000 per cubic millimeter), while on the contrary when administered in the form of benzoate of soda the tendency is to increase the number of red corpuscles in the blood to the same extent. There is also in the latter case a slight increase in the number of white corpuscles.

In one instance in the administration of benzoic acid the number of red corpuscles was increased, while in two instances in the administration of benzoate of soda the number of red corpuscles was decreased. Therefore, in the interpretation of the data these facts must be kept in mind. While the general effect of the benzoic acid appears to be to diminish the number of red corpuscles, and that of the benzoate of soda to increase the number, there are marked exceptions in the individual data. It may be further suggested in this

connection that the tendency to increase the red corpuscles shown by the benzoate of soda may have been due to the increased alkalinity of the blood, induced by the soda, rather than to any specific action of the compound as a whole.

#### NITROGEN METABOLISM.

The percentage data show an increase in the nitrogen excreted both in the urine and in the feces during the preservative period, and there is a decrease in the after period in each case, with the exception of the nitrogen in the feces for those members who received benzoate of soda. While the average data do not show any marked disturbance of the nitrogen metabolism there is a uniform tendency to decrease the nitrogen balance, although the amounts ingested were slightly increased. The average data for the eleven men show an increase of 2 per cent in the preservative period of the amount of ingested nitrogen excreted in metabolized form, indicating a tendency to increase to this extent the katabolic activities, while the increase in the feces points to a decrease in nitrogen assimilation.

#### PHOSPHORIC-ACID METABOLISM.

The summarized data in this case indicate a tendency on the part of the preservative in both forms to increase the percentage of phosphoric acid excreted in the feces, the increase being much more marked in the case of those receiving benzoic acid, the increase in the case of those receiving benzoate of soda occurring chiefly in the after period. There is but little change in the metabolized phosphoric acid excreted in the case of those who received benzoic acid, the percentage data showing a slight decrease in the preservative period and a very marked decrease in the after period. In the case of those who received benzoate of soda there is an increased excretion of phosphoric acid in the urine in the preservative period and a marked decrease in the after period. These figures indicate, therefore, that the benzoic acid, either in the form of the free acid or as benzoate of soda, tends to increase the phosphoric acid in the feces, which effect is continued to a marked degree in the after period. In other words, a decrease in the assimilation of phosphoric acid is produced. On the other hand, there is practically no tendency to increase katabolism in this instance, the slight increase in the excretion in the urine in the case of those receiving sodium benzoate being followed by a marked decrease in the after period to an amount less than in the fore period. There appears to be a slight disturbance of the normal metabolism of phosphoric acid.

## SULPHUR METABOLISM.

These data show in an unmistakable manner that both the benzoic acid and the benzoate of soda increase the excretion in the feces and in the urine, thus establishing the effect of the preservative in decreasing the assimilation of sulphur and slightly increasing the sulphur katabolism. In the case of those receiving benzoic acid there is a tendency in the after period to return to the conditions of the fore period, while in the case of the members who received sodium benzoate there is a further marked increase in the after period. The increased excretion of metabolized sulphur is considered in detail under the special studies on the urine.

TABLE III.—Comparative summary of principal determinations made, Series VIII.<sup>a</sup>

Data.	Benzoic acid (Nos. 1-6). <sup>b</sup>			Sodium benzoate calculated as benzoic acid (Nos. 7-12).		
	Fore period.	Preservative period.	After period.	Fore period.	Preservative period.	After period.
Body weight (kilos)-----	62.10	61.62	61.16	64.24	64.02	63.66
Blood (averages per man):						
Red corpuscles (per cubic mm)-----	5,249,000	4,878,333	5,229,167	4,943,333	5,320,833	5,280,833
White corpuscles (per cubic mm)-----	7,567	7,202	6,583	7,322	7,461	6,104
Composition of feces:						
Weight (grams)-----	74	76	68	74	77	89
Water content (per cent)-----	75.37	74.78	73.84	75.72	76.56	76.72
Dry matter (grams)-----	18	19	18	18	18	21
Urine:						
Volume (cc)-----	997	992	922	1,248	1,206	1,205
Microscopic sediments (per cent of relative occurrence) <sup>c</sup> -----	64.44	75.24	59.13			
Sulphur (as grams SO <sub>3</sub> )—						
Neutral-----	.327	.289	.238	.304	.278	.237
Inorganic-----	1.762	1.840	1.729	1.765	1.855	1.770
Ethereal-----	.158	.156	.148	.155	.152	.139
Total-----	2.247	2.285	2.112	2.223	2.281	2.146
Metabolism (percentage results):						
Nitrogen—						
Nonmetabolized (feces)-----	7.69	8.01	7.68	6.93	7.00	8.54
Metabolized (urine)-----	86.82	87.70	85.61	79.78	82.57	81.69
Phosphoric acid—						
Nonmetabolized (feces)-----	26.56	29.65	29.08	28.59	28.61	34.73
Metabolized (urine)-----	63.66	63.27	58.06	55.95	56.42	52.56
Sulphur—						
Nonmetabolized (feces)-----	9.76	10.58	10.42	8.62	9.23	11.75
Metabolized (urine)-----	79.16	82.19	81.80	73.21	76.78	78.50

<sup>a</sup> Omitting fourth preservative subperiod.<sup>b</sup> Omitting No. 3.<sup>c</sup> Nos. 1 to 12.

## GENERAL CONCLUSIONS.

From a careful study of the data in the individual cases and of the summaries of the results, it is evident that the administration of benzoic acid, either as such or in the form of benzoate of soda, is highly objectionable and produces a very serious disturbance of the metabolic functions, attended with injury to digestion and health.

As in the case of boric acid, salicylic acid, and sulphurous acid, this injury manifests itself in a number of different ways, both in the production of unfavorable symptoms and in the disturbance of



metabolism. These injurious effects are evident in the medical and clinical data, which show grave disturbances of digestion, attended by phenomena which are clearly indicative of irritation, nausea, headache, and, in a few cases, vomiting. These symptoms were not only well marked, but they were produced upon healthy individuals, receiving good and nourishing food and living under proper sanitary conditions. It is only fair to conclude, therefore, that under similar conditions of administration of benzoic acid or benzoate of soda in the case of weaker systems, or less resistant conditions of health, much more serious and lasting injury would be produced.

It was also noticed that the administration of benzoic acid and benzoate of soda was attended with a distinct loss of weight, indicative of either a disturbance of assimilation or an increased activity in those processes of the body which result in destruction of tissue. The production of a loss of weight in cases of this kind must be regarded as indicative of injurious effects.

The influence of the benzoic acid and benzoate of soda upon metabolism was never of a character indicative of a favorable change therein. While often the metabolic changes were not strongly marked, such changes as were established were of an injurious nature. It is evident that the administration of these bodies, therefore, in the food tends to derange metabolism in an injurious way.

An important fact in connection with the administration of these bodies is found in the efforts which nature makes to eliminate them from the system. In so far as possible the benzoic acid is converted into hippuric acid. There is a tendency usually manifested, however, to retain the benzoic acid in the body for a notable length of time, and this is much more marked in the case of benzoate of soda than in the case of benzoic acid.

While the administration of both these bodies, therefore, is undoubtedly harmful, the injurious effects are produced more rapidly in the case of benzoic acid than they are in the case of benzoate of soda: the data, however, will show that the total harmful effect produced in the end is practically the same in both cases; hence there appears to be no reason for supposing that the administration of the preservative in the form of benzoate of soda can be justified by any argument relating to the less injurious effect thereof upon health.

The occurrence of microscopic bodies in the urine is undoubtedly increased under the administration of benzoic acid in both forms, thus showing conclusively the tendency to stimulate the destructive activities of the body.

Coming to the final consideration of all of these different phases of the subject, there is only one conclusion to be drawn from the data



which have been presented, and that is that in the interests of health both benzoic acid and benzoate of soda should be excluded from food products. This conclusion is reached independently of any consideration of the conditions which it is alleged surround the processes of manufacture and which result in the demands of manufacturers to be allowed to continue the use of these substances. This is a subject which must be discussed from an entirely different point of view and has no bearing whatever upon the general conclusions which have been reached, namely, that both benzoic acid and benzoate of soda are bodies which, when added to foods, are injurious to health.

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